

App. No. 10/565,974  
Office Action Dated January 26, 2006

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**Amendments to the Claims:**

This listing of claims will replace all prior versions and listing of claims in the application.

Claims 7, 13 and 15-20 have been canceled without prejudice or disclaimer.

Claims 21-29 are new.

**Listing of Claims:**

At the top of page 35, please insert the phrase We claim:.

1-20. (Canceled)

21. (New) A method of screening a drug for at least one of prevention and treatment of cardiac failure, the method comprising a process of selecting a medicinal component that inhibits apoptosis induced by ASK1 protein and inhibits left ventricular remodeling induced by the ASK1 protein from a drug candidate compound, wherein the process comprises:

administering a drug candidate compound to cells that express a constitutively active mutant of an ASK1 protein or a transgenic mouse that expresses the constitutively active mutant in a heart of the transgenic mouse; and

selecting the medicinal component capable of suppressing apoptosis induced by the ASK1 protein, and

wherein the ASK1 protein is composed of an amino acid sequence of GenBank Database Registration Number D84476.

22. (New) The method of screening according to claim 21, wherein the drug candidate is at least one selected from the group consisting of an anti-ASK1 antibody specific to the ASK1 protein, a dominant negative mutant of the ASK1 protein, and thioredoxin.

23. (New) The method of screening according to claim 21, wherein the constitutively active mutant of the ASK1 protein is ASK1-ΔN, which is a protein lacking amino acids 1 to 648 in the N-terminal region of the ASK1 protein.

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24. (New) A method of screening a drug for at least one of prevention and treatment of cardiac failure, the method comprising a process of selecting a medicinal component that inhibits apoptosis induced by ASK1 protein and inhibits left ventricular remodeling induced by the ASK1 protein from a drug candidate compound, wherein the process comprises:

- collecting or detecting the ASK1 protein from cells in the presence of a drug candidate compound;
- measuring kinase activity of the ASK1 protein in the cells or autophosphorylation of the ASK1 protein in the cells; and
- selecting the medicinal component capable of suppressing the kinase activity of the ASK1 protein or suppressing the autophosphorylation of the ASK1 protein, wherein inhibition of the kinase activity of the ASK1 protein or inhibition of the autophosphorylation of the ASK1 protein is used an indicator for selection, and

wherein the ASK1 protein is composed of an amino acid sequence of GenBank Database Registration Number D84476.

25. (New) The method of screening according to claim 24, wherein the drug candidate is at least one selected from the group consisting of an anti-ASK1 antibody specific to the ASK1 protein, a dominant negative mutant of the ASK1 protein, and thioredoxin.

26. (New) A method of screening a drug for at least one of prevention and treatment of cardiac failure, the method comprising a process of selecting a medicinal component that inhibits apoptosis induced by ASK1 protein and inhibits left ventricular remodeling induced by the ASK1 protein from a drug candidate compound, wherein the process comprises:

- isolating the ASK1 protein or ASK1 mRNA encoding the ASK1 protein from cells or an animal heart in the presence of a drug candidate compound;
- measuring expression of the ASK1 protein or the ASK1 mRNA; and
- selecting the medicinal component capable of inhibiting translation of the ASK1 mRNA or transcription of ASK1 gene encoding the ASK1 mRNA, wherein inhibition of the translation of the ASK1 mRNA or inhibition of the transcription of the ASK1 gene is used as an indicator for selection; and

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wherein the ASK1 protein is composed of an amino acid sequence of GenBank Database Registration Number D84476.

27. (New) A method of screening a drug for at least one of prevention and treatment of cardiac failure, the method comprising a process of selecting a medicinal component that inhibits apoptosis induced by ASK1 protein and inhibits left ventricular remodeling induced by the ASK1 protein from a drug candidate compound, wherein the process comprises:

administering a drug candidate compound to cells in the presence of at least one factor selected from the group consisting of Daxx, TRAF2, and calmodulin-dependent kinase II;

evaluating an activity of the ASK1 protein in the cells; and

selecting the medicinal component capable of inhibiting the at least one factor, wherein inhibition of the ASK1 protein activity is used as an indicator for selection, and

wherein the ASK1 protein is composed of an amino acid sequence of GenBank Database Registration Number D84476.

28. (New) A method of screening a drug for at least one of prevention and treatment of cardiac failure, the method comprising a process of selecting a medicinal component that inhibits apoptosis induced by ASK1 protein and inhibits left ventricular remodeling induced by the ASK1 protein from a drug candidate compound, wherein the process comprises:

administering a drug candidate compound to cells that express a constitutively active mutant of the ASK1 protein in a heart;

evaluating activity of at least one factor selected from the group consisting of MKK3, MKK4, MKK6, MKK7, JNK, and p38MAPK; and

selecting the medicinal component capable of inhibiting the at least one factor activated by the ASK1 protein, wherein inhibition of the at least one factor activated by the ASK1 protein is used as an indicator for selection, and

wherein the ASK1 protein is composed of an amino acid sequence of GenBank Database Registration Number D84476.

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29. (New) The method of screening according to claim 28, wherein the constitutively active mutant of the ASK1 protein is ASK- $\Delta$ N, which is a protein lacking amino acids 1 to 648 in the N-terminal region of the ASK1 protein.